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PRE-APPEAL BRIEF REQUEST FOR REVIEW	Docket Number (Optional) 273012012500	
	Application Number 10/072,272	Filed February 6, 2002
	First Named Inventor H. Andrew STRONG	
	1617	Examiner Y.S. Chong

Applicant requests review of the final rejection in the above-identified application. No amendments are being filed with this request.

This request is being filed with a Notice of Appeal. A final rejection was mailed 11 June 2008. A Notice of Appeal was therefore due 11 September 2008.

The review is requested for the reason(s) stated on the attached sheet(s).
Note: No more than five (5) pages may be provided.

I am the

- [ ] applicant /inventor.
- [ ] assignee of record of the entire interest. See 37 CFR 3.71. Statement under 37 CFR 3.73(b) is enclosed. (Form PTO/SB/96)
- [x] attorney or agent of record. Registration number 54,403
- [ ] attorney or agent acting under 37 CFR 1.34. Registration number if acting under 37 CFR 1.34.

/Leslie A. Robinson/
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October 14. 2008
Date

NOTE: Signatures of all the inventors or assignees of record of the entire interest or their representative(s) are required. Submit multiple forms if more than one signature is required, see below*.

[x] *Total of 1 forms are submitted.

sd-445077

Pre-Appeal Brief Request for Review

The claims at issue encompass the use of photodynamic therapy (PDT) to treat occult choroidal neovascular (CNV) lesions in a specific sub-population of patients having an occult component of the CNV lesion that is >50% and <100% of the lesion, and assessed as having either (a) a small lesion size, or (b) poor visual acuity prior to treatment, or both. Although the use of PDT to treat patients having predominantly classic CNV lesions is known in the art (TAP Report 1, *Arch. Ophthalmol.* 1999; 117:1329-1345; hereinafter "TAP Report 1"), the selection of a specific sub-population of patients having occult CNV for which PDT treatment would be beneficial was not known before the present invention. This aspect of the claimed invention makes it both valuable and nonobvious, as it allows the identification and treatment of a patient population for which the prior art would not have predicted efficacy.

The outstanding rejections are for obviousness. The obviousness rejection of each claim relies upon a single primary reference, the TAP Report 1, alone or in combination with a secondary reference, to Zeimer et al. (U.S. Patent No. 5, 935,942). Applicants believe the rejections are improper. Applicants request this review for the following reasons:

Reason 1: The rejection improperly disregards express claim limitations.

The claims require the selection of a subject having an occult CNV lesion where (1) the occult component is >50% and <100% of the lesion, and (2) the subject is assessed as having either (a) a small lesion size, or (b) poor visual acuity prior to treatment, or both (a) and (b).

While asserting that the TAP Report 1 describes each of these three parameters (percent occult component, lesion size, and visual acuity) separately, the Examiner erroneously concludes that the selection of a sub-population of patients having a combination of specific features within each of these parameters is obvious. The Examiner appears to be arguing that the claimed sub-population is inherently somewhere amongst the verteporfin treatment population, while completely dismissing the express teachings of the TAP Report 1 that CNV lesions having an occult component of >50% and <100% of the lesion (an express feature of the rejected claims) are non-responsive to verteporfin treatment. Applicants respectfully submit that the TAP Report 1, considered in its entirety including the portions that would lead away from the claimed invention, fails to render the claimed methods obvious.

The Examiner points to Table 2 of the TAP Report 1, which reports "Evidence of occult CNV" in 305 of 402 verteporfin-treated eyes, without specifying the percent occult component, and further reports that 199 of the treated eyes had poor visual acuity. The Examiner concludes that at least about 100 verteporfin-treated patients "had evidence of Occult CNV with visual acuity of less than 65." In addition, the Examiner contends that because certain patients in the verteporfin treatment group had small lesions of less than 6 disc areas, that "the population who showed Occult CNV in the TAP Report and further received verteporfin, are the same as the instantly claimed population." Thus, the Examiner concludes that "the instantly claimed intended purpose is inherently achieved."

As described in Table 2 of the TAP Report 1, only 201 patients in the verteporfin treatment group had a lesion composed of >0 to <50% classic CNV (i.e., >50 to < 100% occult CNV as featured in the claims), and no correlation between these patients and those having poor visual acuity and/or small lesion size is provided. Thus, contrary to the Examiner's conclusion, no evidence has been provided to demonstrate that the claimed sub-population is inherently present among the patients in the verteporfin treatment group of the TAP Report 1. It is well settled law that "[t]o establish inherency, the extrinsic evidence must make clear that the missing descriptive matter is *necessarily* present in the thing described in the reference, and that it would be so recognized by persons of ordinary skill." MPEP § 2112 (IV). Inherency may not be established by probabilities or possibilities, as the Examiner is attempting to do in this case. *Id.*

As discussed above, the invention as claimed requires the selection of patients having an occult component of >50% and <100% of the lesion and assessed as having either small lesion size, poor visual acuity, or both. Applicants respectfully point out that the alleged "evidence of occult CNV" does not satisfy the claim limitation that the occult component be >50% and <100% of the lesion, and the cited reference simply provides no guidance that would lead to the selection of the claimed sub-population of patients having occult CNV lesions with this percent occult component *in combination with* small lesion size and/or poor visual acuity.

Even assuming, *arguendo*, that some of the verteporfin-treated patients in the TAP Report 1 study did fall within the claimed sub-population, this alone is insufficient to render the claimed methods obvious when the TAP Report 1 provides no guidance or motivation that would

lead one of skill in the art to recognize and select such a sub-population of patients for whom treatment would be beneficial.

Reason 2: The rejection does not view the prior art from the perspective of one of ordinary skill.

The proper determination of obviousness must be made from the perspective of a person of ordinary skill in the relevant art in view of the cited references and the person's general skills and knowledge. In the instant case, the Examiner insists that in view of the TAP Report 1, it would have been obvious to one of ordinary skill in the art to treat patients having an occult CNV lesion with an occult component within the claimed range. The Examiner has maintained this position despite repeated statements by the study's authors that PDT is ineffective for such patients, and the lack of any guidance regarding additional features that might confer responsiveness to PDT in such patients.

The Examiner acknowledges that the results in Table 5 of the TAP Report 1 show no benefit and no appreciable difference from placebo for patients with lesions having an occult component within the claimed range of >50% and <100%. Nevertheless, the Examiner insists that because of the benefit to patients with ≥50% classic CNV (i.e., ≤50% occult CNV) and with 0% classic CNV (i.e., 100% occult CNV), it would have been obvious to one of ordinary skill in the art to treat patients with lesions having an occult component within the outer limits of the claimed range "due to routine experimentation and optimization," and that one of ordinary skill in the art would have had a reasonable expectation of success in treating such patients.

The Examiner has provided no basis to support the contention that one of ordinary skill in the art would disregard a major finding of the TAP Report 1 study and attempt "optimization" of the conditions for the treatment of lesions where the reference teaches that PDT treatment is ineffective. This assertion by the Examiner is contradicted by actual data presented in the TAP Report 1 and its interpretation by the study's authors.

Moreover, the Examiner has disregarded the data presented in Table 2 of the instant application, which demonstrate that poor results were achieved 24 months after verteporfin

treatment for patients having occult CNV lesions who did not have poor visual acuity at baseline or small lesion size. *See* the specification at page 45, Table 2.

In view of the numerous statements made by the authors of the TAP Report 1 that PDT is ineffective in patients with a CNV lesion having a significant occult character and the presence of patients with classic CNV lesions in the treatment group, a person of ordinary skill in the art would reasonably attribute the verteporfin-responsiveness of the treatment group to those patients having ≥50% classical CNV (less than 50% occult CNV). The TAP Report 1 simply provides no guidance that would lead one of skill in the art to select the claimed sub-population, and therefore, the reference would not provide a person of skill in the art with either a reasonable expectation of success or any motivation to practice the instantly claimed methods.

Reason 3: The Examiner has improperly disregarded the nonobviousness of the invention as a whole.

"In determining the differences between the prior art and the claims, the question under 35 U.S.C. 103 is not whether the differences themselves would have been obvious, but whether the claimed invention as a whole would have been obvious." MPEP § 2141.02 (II).

The Examiner's obviousness analysis has improperly focused on a single element of the claims, i.e., the percent occult component of the CNV lesion, rather than on the obviousness of the invention as a whole. The Examiner has disregarded the essence of the present invention – namely, the selection of a sub-population of occult CNV patients having lesions with >50% and <100% occult component, and including the *additional criteria* of small lesion size, or poor visual acuity, or both, for which PDT treatment is surprisingly beneficial.

As noted above, the TAP Report 1 does not provide a correlation between the percent occult character of the CNV lesion and the patient's visual acuity or lesion size, and there is no evidence that demonstrably proves that the claimed sub-population is even present in the study. Thus, there is simply no basis for the Examiner's assertion that the selection of the specific sub-population of occult CNV patients, as claimed, would have been obvious in view of the TAP Report 1. Because nothing in the cited reference would lead one of skill in the art to the invention as claimed, Applicants respectfully submit that the TAP Report 1 does not render the claimed invention obvious.

Reason 4: The claimed invention provides unexpected advantages that overcome any allegation of obviousness.

The Examiner also improperly ignored evidence of an effect that is entirely unexpected in view of the prior art. The data presented in the specification demonstrate an unexpected and advantageous improvement in visual acuity in patients having CNV lesions that are substantially occult in character and having either small lesion size or poor visual acuity prior to treatment, with an enhanced improvement in visual acuity for patients having both of these additional characteristics. *See* the specification at page 45, Table 2.

The prior art does not provide any reason to expect that the treatment of this sub-population would be beneficial, in view of the teachings of the TAP Report 1 that PDT is ineffective in patients having an occult component in the claimed range, and the lack of information regarding additional features that would render such treatment beneficial. The combination of the TAP Report 1 with Zeimer et al. does not remedy this deficiency in the Examiner's *prima facie* case. This unexpected effect is the core of the claimed invention, commensurate with the scope of the claims, and demonstrates that the invention as a whole is nonobvious.

In view of the remarks above, the invention as claimed is not rendered *prima facie* obvious by the cited references. Even if a *prima facie* case for obviousness were established, this unexpected effect achieved by the claimed invention overcomes any allegation of obviousness. The obviousness rejection is overcome and should be withdrawn.

Dated: October 14, 2008

Respectfully submitted,

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